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09/284,180	06/09/1999	TORU KIMURA	20-4546P	1992

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EXAMINER
CHEN, SHIN LIN

ART UNIT	PAPER NUMBER
1632	

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33

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/284,180	Kimura et al.
Examiner	**Art Unit**
Shin-Lin Chen	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *2-19-03 and 3-24-03*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *34, 41, 42, 48-52, and 56-61* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☒ Claim(s) *34* is/are allowed.

6) ☒ Claim(s) *41, 42, 48-52, and 56-61* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 29
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicants' amendment and declaration filed 2-19-03 and amendment filed 2-24-03 have been entered. Claims 41 and 51 have been amended. Claims 56-61 have been added. Claims 34, 41, 42, 48-52 and 56-61 are pending and under consideration.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 41, 42, 48-50, 56, 57, 60 and 61 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims read on an isolated nucleic acid comprising a polynucleotide that specifically hybridizes with a complement of SEQ ID No. 1 or SEQ ID No. 2 or has at least 80% or 90% homology to SEQ ID No. 1 or 2 under the hybridization and washing conditions cited in the claims and encodes a protein having the biological activity of inhibiting neurite outgrowth from dorsal root ganglion cells or collapsing growth cones of retinal ganglion cells, an expression plasmid comprising said nucleic acid, a host cell comprising said expression plasmid, and a process for producing a recombinant protein by using said host cell.

Kennel, 1971 (Progr. Nucl. Acid Res. Mol. Biol., Vol. 11, p. 259-301) states that formation of a stable complex between two polynucleotides depends on G+C content and the minimum size for a stable complex is from 10 to 20 nucleotides. "The thermal stability rises sharply for longer lengths so that, depending on the G+C content, the stability of a complementary duplex of 25-50 nucleotides approaches that of any much longer complex" (see page 261). Any polynucleotide sequence having at least 25-50 nucleotides, depending on G+C content, identical to SEQ ID No. 1 or 2 would be able to hybridize to the sequence of SEQ ID No. 1 or 2 under the hybridization condition cited. A polynucleotide that is 80% or 90% identical to SEQ ID No. 1 or 2 has at least 800 or 400 nucleotide difference (as compared to SEQ ID No. 1) and at least 460 or 230 nucleotide difference (as compared to SEQ ID No. 2) from the sequence of SEQ ID No. 1 and 2, respectively. Thus, the claims encompass natural and **synthetic** polynucleotide sequences that are vastly different from SEQ ID No. 1 or 2 and various nucleic acids having unknown nucleotide sequences adding to 5', 3' and/or within the sequence of SEQ ID No. 1 or 2. The specification of the present application only disclosed the nucleotide sequences of SEQ ID Nos. 1 and 2 (rat semaphorin W) and the amino acid sequence deduced from SEQ ID No. 2 (SEQ ID No. 3), and the nucleotide sequences of human semaphorin W cDNA (SEQ ID Nos. 4, 5, 7 and 10).

The scope of the claims includes various unknown and unidentified nucleic acids encoding proteins that are totally different from the protein encoded by SEQ ID No. 1 or 2 and a genus of numerous structural variants of the disclosed semaphorin W protein (SEQ ID No. 3) and

having the biological activity of inhibiting neurite outgrowth from dorsal root ganglion cells or collapsing growth cones of retinal ganglion cells, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification only discloses the homologies of the primary amino acid sequences in semaphorin domain among the known semaphorin genes are 20-80% and not necessarily high (specification, page 4, lines 17-20), and **suggest** that the amino acid residue at position 204 of SEQ ID No. 3 could be essential to the activity of semaphorin protein (specification, page 18, lines 17-22). The post-filing documents accompanied with the preliminary amendment filed 11-20-01 indicates that the human semaphorin cDNA sequence is 82.4% identical to the rat semaphorin cDNA sequence and the overall degree of amino acid sequence identity is 90.6%.

The claimed nucleic acids could be totally different from or could vary dramatically from the disclosed nucleotide sequences, i.e. SEQ ID Nos. 1 and 2, of the present application. Although the human semaphorin cDNA is 82.4% identical to rat semaphorin W cDNA and the method for making variant nucleic acids and assays for identifying protein having the claimed biological activity were known in the art, the scope of the claims encompasses unknown and unidentified genes having nucleotide sequence that is drastically different from the sequence of SEQ ID No. 1 or 2 but do not have the claimed biological activity. There is no nexus between the polynucleotide, that hybridizes with SEQ ID No. 1 or 2 under the cited hybridization condition or at least 80% or 90% identical to SEQ ID No. 1 or 2 under the cited hybridization condition, and the encoded protein that has the biological activity of inhibiting neurite outgrowth

from dorsal root ganglion cells or collapsing growth cones of retinal ganglion cells. There is no evidence of record that the proteins encoded by the semaphorin gene family all have the same biological function as the rat semaphorin W (SEQ ID No. 3) of inhibiting neurite outgrowth from dorsal root ganglion cells or collapsing growth cones of retinal ganglion cells. A few conserved amino acid residues does not necessarily mean that they all have same biological functions.

Further, the specification indicates that ""semaphorin domain" refers to a domain consisting of 300-600 amino acid residues more than 20% of which are identical to those amino acids constituting the semaphorin domain of any one of ten known semaphorins" and thirteen cysteines are conserved in semaphorin domain of the ten known semaphorins (Specification, page 23, lines 10-13 and 22-24). The amino acid sequences between semaphorin domains of the known semaphorins could differ from 240-480 amino acid residues which account to 720-1440 nucleotide difference among the known semaphorin domains. The identical amino acid residues among semaphorin domains of the known semaphorin are not necessarily identical throughout all known semaphorin rather they are identical to a certain subgroups of the known semaphorins. Therefore, no common structural feature of the nucleic acids encoding proteins having the activity of inhibiting neurite outgrowth from dorsal root ganglion cells or collapsing growth cones of retinal ganglion cells has been disclosed in the specification. The specification fails to provide sufficient description that applicants had possession of the full scope of the nucleic acids at the time of the invention.

The sequence search results cited in the amendment filed 2-19-03 shows 58 kinds of sequence hit which **should have** at least 80% homology to SEQ ID No. 2 (amendment, p. 13) but the data does not show whether applicants have possession of those sequences. It is not clear what those sequences are, whether those sequence have at least 80% identity to SEQ ID No. 1 or 2, and whether those sequences were disclosed before the time of the present invention. Thus, one skilled in the art at the time of the invention would not know whether applicants have possession of those sequences at the time of the invention.

This limited information disclosed in the present application is not sufficient to reasonably convey to one skilled in the art that applicants were in possession of the claimed nucleic acids. Thus, it is concluded that the written description requirement is not satisfied for the nucleic acids that encode the genus of proteins discussed above.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

With the exception of the sequences referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides, and therefore conception is not achieved regardless of the complexity or simplicity of the method of isolation. Adequate

written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only the disclosed SEQ ID Nos. 1-3, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Applicants cite example 9 of written description training materials and argue that eh hybridization condition cited in the claims is high stringency condition (amendment, p. 10-12). This is not found persuasive because of the reasons set forth above and that example 9 is just an example to explain written description guideline and the patentability of each patent application has to be considered case by case.

Applicants cite sequence search that results in 58 kinds of sequence hit, which should have at least 80% homology to SEQ ID No. 2 (amendment, p. 12-13). This is not found persuasive because of the reasons set forth above.

3. Claims 41, 42, 48-50 and 56-61 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated DNA comprising SEQ ID No. 1 or 2 and a DNA encoding a polypeptide sequence of SEQ ID No. 3 that functions to inhibit neurite outgrowth, does not reasonably provide enablement for any isolated nucleic acid comprising a polynucleotide that specifically hybridizes with a complement of SEQ ID No. 1 or SEQ ID No. 2, or said polynucleotide has at least 80% or 90% homology to SEQ ID No. 1 or 2 under the hybridization and washing conditions cited in the claims and encodes a protein having the biological activity of inhibiting neurite outgrowth from dorsal root ganglion cells or collapsing growth cones of retinal ganglion cells, a nucleic acid comprising the nucleotide sequence of SEQ ID No. 5 or 10 and has the cited biological activity, an expression plasmid comprising said nucleic acid, a host cell comprising said expression plasmid, and a process for producing a recombinant protein by using said host cell. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims are directed to an isolated nucleic acid comprising a polynucleotide that specifically hybridizes with a complement of SEQ ID No. 1 or SEQ ID No. 2 or has at least 80% or 90% homology to SEQ ID No. 1 or 2 under the hybridization and washing conditions cited in the claims and encodes a protein having the biological activity of inhibiting neurite outgrowth from dorsal root ganglion cells or collapsing growth cones of retinal ganglion cells, a nucleic acid comprising the nucleotide sequence of SEQ ID No. 5 or 10 and has the cited biological activity,

an expression plasmid comprising said nucleic acid, a host cell comprising said expression plasmid, and a process for producing a recombinant protein by using said host cell.

As discussed above, any polynucleotide sequence having at least 25-50 nucleotides, depending on G+C content, identical to SEQ ID No. 1 or 2 would be able to hybridize to the sequence of SEQ ID No. 1 or 2 under the hybridization condition cited. A polynucleotide that is 80% or 90% identical to SEQ ID No. 1 or 2 has at least 800 or 400 nucleotide difference (as compared to SEQ ID No. 1) and at least 460 or 230 nucleotide difference (as compared to SEQ ID No. 2) from the sequence of SEQ ID No. 1 and 2, respectively. Thus, the claims encompass **natural and synthetic** polynucleotide sequences that are vastly different or totally different from SEQ ID No. 1 or 2 and various nucleic acids having unknown nucleotide sequences adding to 5', 3' and/or within the sequence of SEQ ID No. 1 or 2. The specification of the present application only disclosed the nucleotide sequences of SEQ ID Nos. 1 and 2 (rat semaphorin) and the amino acid sequence deduced from SEQ ID No. 2 (SEQ ID No. 3), and the nucleotide sequences of human semaphorin cDNA (SEQ ID Nos. 4, 5, 7 and 10). The scope of the claims include various unknown and unidentified nucleic acids encoding a genus of numerous structural variants, derived from different organisms including humans, cows, dogs, mice, whales, fish, insects, plants etc., of the disclosed semaphorin protein (SEQ ID No. 3), and the genus is highly variant because a significant number of structural differences between genus members is permitted.

Nucleotide difference at every 5 or 10 nucleotide position within a polynucleotide sequence can result in a polynucleotide encoding a totally different protein from the amino acid

sequence of SEQ ID No. 3. Polynucleotides that are at least 80% or 90% identical to SEQ ID No. 1 or 2 and hybridize to SEQ ID No. 1 or 2 under the cited hybridization condition could still have about 230 to 800 nucleotide difference from SEQ ID No. 1 or 2, and the proteins encoded by said polynucleotides could differ dramatically from SEQ ID No. 3 and have totally different protein functions from SEQ ID NO. 3. Polynucleotide sequence that only has 50 nucleotides identical to SEQ ID No. 1 or 2 (SEQ ID No. 1 contains 5' and 3' untranslated sequences) can hybridize to SEQ ID No. 1 or 2 but the protein encoded by said polynucleotide sequence would be totally different from SEQ ID No. 3 and would have different biological function from SEQ ID No. 3. Further, SEQ ID No. 5 and 10 are partial human cDNA sequences. A polynucleotide comprising either SEQ ID No. 5 or 10 encompasses adding unknown sequence to 5' and 3' end of SEQ ID No. 3 or 5 and said polynucleotide can encode protein differ dramatically from SEQ ID No. 3. Thus, the claimed nucleic acids, which include natural and synthetic nucleic acids, could encode proteins that are totally different or drastically different from SEQ ID No. 3 and would not have the biological function of SEQ ID No. 3. One skilled in the art at the time of the invention would require trial and error experimentation to identify the proteins, to characterize the properties of said proteins, and to determine the biological function of said proteins.

The specification fails to provide adequate guidance for a domain or a region within a semaphorin that contributes to any functional characteristic of the semaphorin having the sequence of SEQ ID No. 3. The cited reference Kolodkin et al, 1993, only shows there is a semaphorin gene family but fails to show whether those genes encode proteins having same

biological functions, such as inhibiting neurite outgrowth from dorsal root ganglion cells or collapsing growth cones of retinal ganglion cells. There is no evidence of record that the proteins encoded by the semaphorin gene family all have the same biological function as the rat semaphorin W (SEQ ID No. 3) of inhibiting neurite outgrowth from dorsal root ganglion cells or collapsing growth cones of retinal ganglion cells. A few conserved amino acid residues does not necessarily mean that they all have same biological functions. There is no indication of regions or specific amino acids within the semaphorin family proteins, except aspartic acid at position 198 of Sema III protein, where mutations or variations would be tolerated without any change of the functional characteristic of the semaphorin and regions where they would not be tolerated. The specification presumes glutamic acid at position 204 of SEQ ID No. 3 and glutamic acid at position 16 of SEQ ID No. 6 correspond to aspartic acid at position 198 of Sema III, however, there is no evidence of record that glutamic acid at position 204 of SEQ ID No. 3 and glutamic acid at position 16 of SEQ ID No. 6 play an essential role in the biological function of rat and human smaphorin proteins, respectively.

The amino acid sequence of a protein determines its structural and functional properties, and predictability of which amino acids can be removed from a protein's sequence and still result in similar activity is extremely complex, and well outside the realm of routine experimentation, because accurate predictions of a protein's structure from mere sequence data are limited. Rudinger, 1976 (W) points out that "The significance of particular amino acids and sequences for different aspects of biological activity cannot be predicted *a priori* but must be determined from

case to case by painstaking experimental study" (e.g. p. 6). Kaye et al., 1990 (Proc. Natl. Acad. Sci. USA, Vol. 87, pp. 6922-6926) discloses that a single amino acid substitution results in a retinoblastoma protein defective in phosphorylation and oncoprotein binding (e.g. title). Skolnick et al., 2000 (Trends in Biotech, Vol. 18, p. 34-39) states "Sequence-based methods for function prediction are inadequate because of the multifunctional nature of proteins. However, just knowing the structure of the protein is also insufficient for prediction of multiple functional sites. Structural descriptors for protein functional sites are crucial for unlocking the secrets in both the sequence and structural-genomics projects" (e.g. abstract). Skolnick further states that "Knowing a protein's structure does not necessarily tell you its function" and "Because proteins can have similar folds but different functions, determining the structure of a protein may or may not tell you something about its function" (e.g. p. 36, box 2). Therefore, one skilled in the art at the time of the invention would not be able to predict the function of a protein merely from the amino acid sequence of said protein. In view of such, the unpredictability of the biological function of a protein, and the lack of detailed information regarding the structural and functional requirements of a semaphorin, it would be unpredictable at the time of the invention whether the proteins encoded by the claimed nucleic acids would have the functional characteristic of the amino acid sequence of SEQ ID No. 3.

Therefore, it is concluded that based upon the nature of the claimed invention, the state of the art, the unpredictability found in the art, the teaching and working examples provided, and

the breadth of the claims that one skilled in the art at the time of the invention would have had to engage in undue experimentation to practice over the full scope of the invention claimed.

Applicants argue that it is improper to rely solely on "unpredictability" in maintaining enablement rejection, and using the disclosed sequence of the present invention as starting materials to perform mutation and screening experiment by methods known in the art would be routine experimentation (amendment, p. 15). This is not found persuasive because of the reasons set forth above under 35 U.S.C. 112 first paragraph enablement rejection section. "Unpredictability" is not the only Wands factor that have been addressed in previous and present Official actions, for example, the breadth of the claims, the nature of the invention, the state of the prior art, the amount of direction provided by the inventor, and the level of predictability in the art, all have been discussed in those Official actions. However, "unpredictability" is one of the most important factor that requires one of skilled in the art at the time of the invention undue experimentation to practice over the full scope of the invention claimed. As discussed above, the claims encompass **natural and synthetic** polynucleotide sequences that are vastly different or totally different from SEQ ID No. 1 or 2 and various nucleic acids having unknown nucleotide sequences adding to 5', 3' and/or within the sequence of SEQ ID No. 1 or 2. There is no evidence of record that the proteins encoded by the semaphorin gene family all have the same biological function as the rat semaphorin W (SEQ ID No. 3) of inhibiting neurite outgrowth from dorsal root ganglion cells or collapsing growth cones of retinal ganglion cells. A few conserved amino acid residues does not necessarily mean that they all have same biological functions. There is no

indication of regions or specific amino acids within the semaphorin family proteins, except aspartic acid at position 198 of Sema III protein, where mutations or variations would be tolerated without any change of the functional characteristic of the semaphorin and regions where they would not be tolerated. The specification presumes glutamic acid at position 204 of SEQ ID No. 3 and glutamic acid at position 16 of SEQ ID No. 6 correspond to aspartic acid at position 198 of Sema III, however, there is no evidence of record that glutamic acid at position 204 of SEQ ID No. 3 and glutamic acid at position 16 of SEQ ID No. 6 play an essential role in the biological function of rat and human smaphorin proteins, respectively. One skilled in the art at the time of the invention would not be able to predict the function of a protein from mere amino acid sequence of said protein. Thus, one skilled in the art would require undue experimentation to practice over the full scope of the invention claimed.

Applicants cite reference Kolodkin et al., 1993, and argue that semaphorin gene family contain several conserved amino acid residues and on of ordinary skill in the art would know which residue should not be modified (amendment, p. 16). This is not found persuasive because of the reasons set forth above under 35 U.S.C. 112 first paragraph enablement rejection section.

4. Claims 51 and 52 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 51 and 52 are directed to an isolated nucleic acid consists of a single-stranded polynucleotide consisting of at least 27 contiguous nucleotides of SEQ ID No. 2, 4, or 10 and said nucleic acid does not consist of a polynucleotide consisting of at least 27 nucleotides of SEQ ID No. 15, nucleotides 1141-1170 or 1287-1361 of SEQ ID No. 2, and nucleotides 488-816 of SEQ ID No. 4. The phrase "an isolated nucleic acid... consisting of at least 27 contiguous nucleotides of SEQ ID No. 2, 4, or 10 and said nucleic acid does not consist of a polynucleotide consisting of at least 27 nucleotides of SEQ ID No. 15, nucleotides 1141-1170 or 1287-1361 of SEQ ID No. 2, and nucleotides 488-816 of SEQ ID No. 4" is considered new matter. The specification only provide description of a DNA that hybridizes under stringent conditions to DNA comprising at least part of rat or human semaphorin DNA shown in SEQ ID No. 1, 4, or 10 (specification, p. 27, lines 20-24). The specification fails to provide sufficient description for the phrase set forth above, therefore, the subject matter of claims 51 and 52 are considered new matter.

Conclusion

Claims 41, 42, 48-52 and 56-61 are rejected. Claim 34 is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (703) 305-1678. The examiner can normally be reached on Monday to Friday from 9 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds can be reached on (703) 305-4051. The fax phone number for this group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

Shin-Lin Chen, Ph.D.